Equine Pericardium for Tectonic Repair of Corneal Perforations

Aknowledgements:

We have no conflicts of interest or any source of funding to declare.

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INTRODUCTION

Corneal perforation can be the result of trauma, severe burn or corneal ulcerative disease. It can cause devastating acute complications, which in the longer term can lead to phthisis and blindness. Therefore, promt diagnosis and management of this ophthalmologic emergency is crucial in order to maintain globe integrity. [1]

Several factors determine optimal management; the cause of perforation, size and location of the defect, as well as extent of stromal and scleral involvement. Smaller corneal perforations can be adressed with a bandage contact lens, tissue adhesives, conjuctival flaps or amniotic membrane transplantation, whereas larger perforations may require patching with more stable materials, such as scleral and corneal allografts. [1]

Human corneal or amniotic membrane grafts are not always available, necessitating the need for alternative biomaterials when facing emergencies. Pericardium is a collagen-rich biological tissue widely used as a biomaterial for tissue enginneering applications, mostly the construction of bioprostheses in neurosurgery and cardiovascular surgery. In ophthalmic surgery, bovine and human donor pericardium has been applied for the management of exposed glaucoma shunts [2-4] and orbital implants [5,6] as well as scleral thinning. [7] Recently, the use of bovine pericardium for the urgent management of corneal perforations was reported. [8,9]

Equine pericardium has been assessed or is currently used in clinical practice, e.g. as a dura substitute in neurosurgery, [10] for reconstruction of calcified mitral annulus and aortic aneurysms in cardiovascular surgery [11,12] and for treating bone defects in dental surgery, [13,14] however, to our knowledge there is no report to date on the use of this novel biomaterial in ophthalmic surgery. Herein, the successful use of equine pericardium for sealing corneal perforations is described.

CASE PRESENTATION

A 38-year old male was referred to our department with a bilateral non-infectious perforated corneal melt due to presumed ocular nonsteroidal anti-inflammatory drugs (NSAID) abuse. The patient reported regular chronic use of 'unknown' eye drops, without medical monitoring, for his chronic bilateral eye irritation. He denied any previous ocular surgery, while his medical history was insignificant.

Visual acuity was hand motion in both eyes. No lid or lash abnormalities were present. Slit lamp biomicroscopy showed a moderate conjuctival injection and a bilateral melting of the inferior half of the cornea. A mild inflammatory stromal infiltrate surrounded the area of ulceration, while a focal perforation of approximately 4mm caused iris prolapse and athalamia **(Figures 1a and b)**. Intraocular pressure, estimated digitally, was in hypotonic levels. Ophthalmoscopy showed an unremarkable fundus in the periphery, B-scan revealed normal posterior segment findings.

As amniotic membrane or corneal allografts were not readily available, we decided to use lyophilized equine pericardium to seal the corneal defect temporarily and delay corneal grafting until control of the associated inflammation would allow survival of the graft. Informed consent was obtained from the patient prior to surgery. The procedure was performed under topical anaesthesia. According to the manufacturer's recommendations, the dry patch was moistened in physiological saline solution for 1 minute to soften and recover its original consistency. After debriding the necrotic tissue, the extent of the defect was measured and the pericardium sheet (40 mm x 50 mm) was trimmed to the appropriate size and shape and fixated with interrupted 10-0 Nylon stitches **(Figures 1c and d)**. Cultures and corneal tissue specimens were additionally obtained for microbiological and histopathological examination. Finally, cefuroxime at a concentration of 1mg/0.1ml was injected into the anterior chamber. During the postoperative period, oral and local antibiotic as well as local anti-inflammatory treatment was given. Both eyes were regularly treated with preservative-free lubricating eye drops. The patient was examined on a daily basis for signs of infection or hypotony. Intraocular pressure was carefully estimated digitally. Bacterial and fungal cultures were

negative, whereas the histopathological examination did not provide any specific findings apart from the presence of neutrophils.

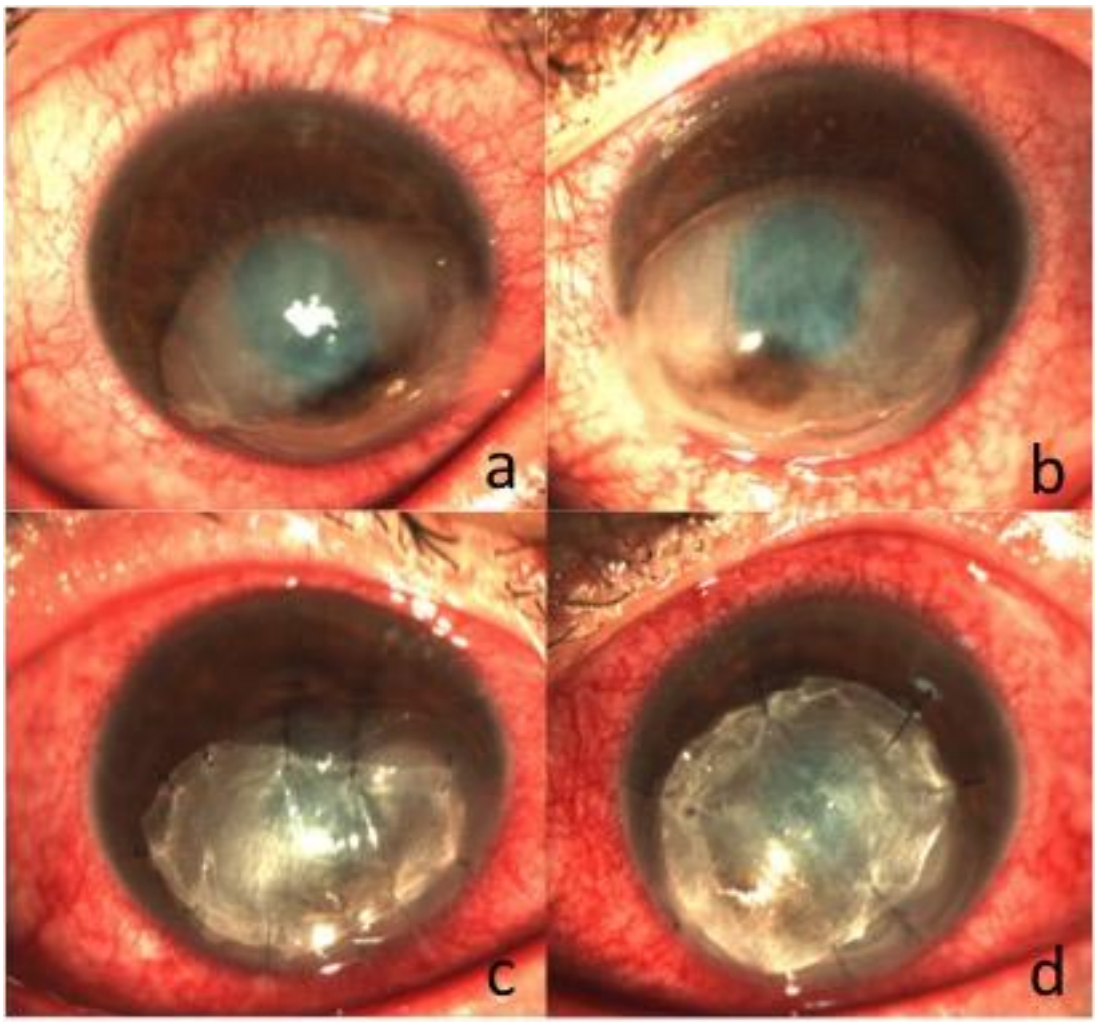

Fig. 1 Photo collage of slit-lamp pictures of both eyes. Perforated corneal melt causing iris prolapse and athalamia in the right (OD) **(a)** and left eye (OS) **(b)** at presentation. Management of the perforation with a single layer of equine pericardium fixated with nylon 10-0 sutures OD **(c)** and OS **(d)**

An immediate watertight closure of the corneal perforation was achieved and maintained throughout an observation period of 6 months with no evidence of infection or recurrent melting. The intraocular pressure remained stable and the patient did not complain about pain or significant discomfort.

A self-limiting partial degradation of the pericardium and loosening of sutures was observed at 2 months in both eyes **(Figures 2a and b)**. During suture removal, the pericardium dislodged exposing tectonically stable vascularized scars **(Figures 2c and d)**.

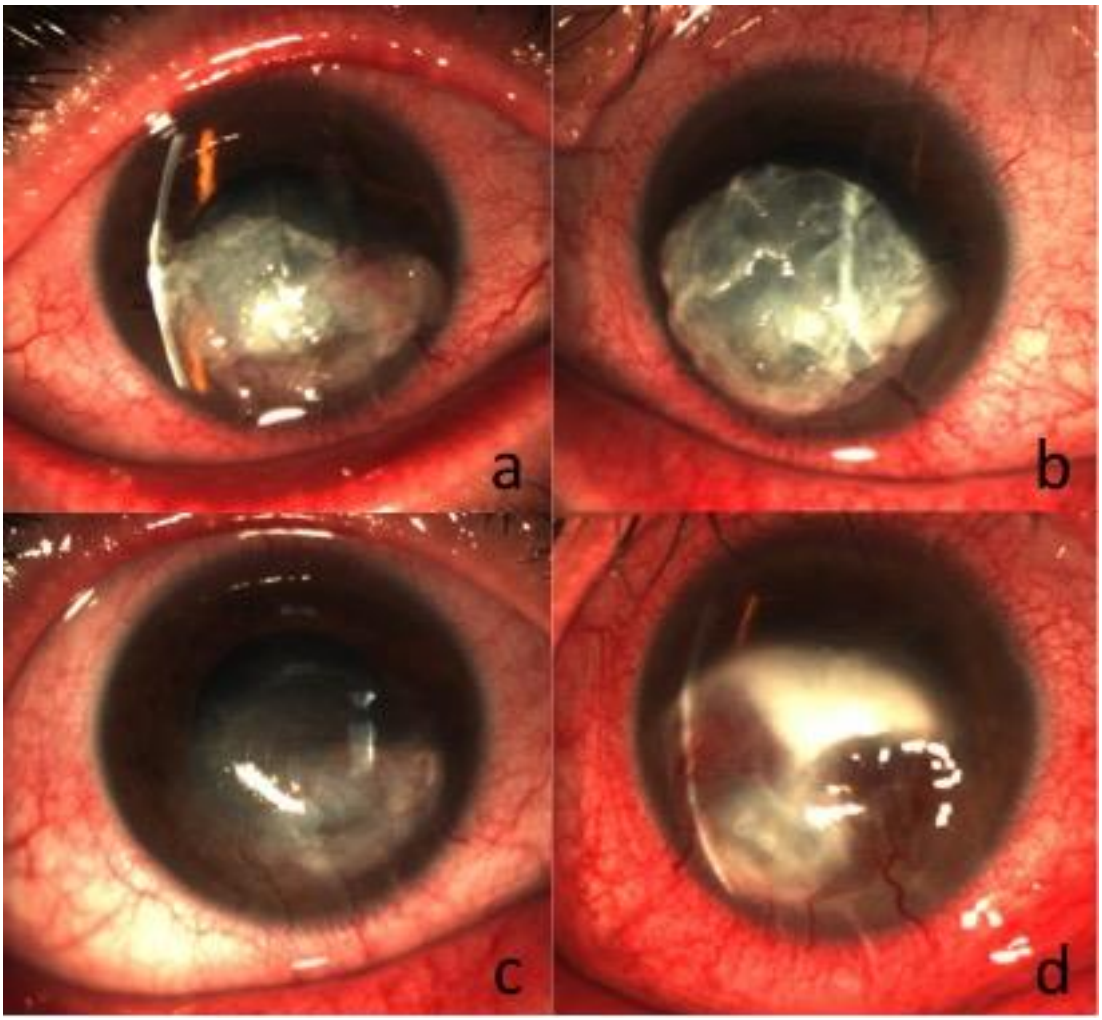

Fig. 2 Partial degradation of the pericardium at 2 months OD **(a)** and OS **(b)** and a tectonically stable vascularized scar 5 months after surgery OD **(c)** and OS **(d)**.

DISCUSSION

The successful employment of lyophilized equine pericardium for the urgent management of non-infectious corneal perforations is reported. This is to our knowledge the first report on the use of this reconstructive biomaterial in ophthalmic surgery.

Equine pericardium undergoes industrial processing prior to transplantation; the cellular components of the tissue are removed (decellularization) through physical, enzymatic or chemical treatments resulting in an antigenically neutral biomaterial, while the integrity of the extracellular matrix is preserved. The purified collagen network is then fortified by means of cross-linking, coating with biopolymeric films or lyophilization (freeze drying). Finally, it is chemically sterilized and irradiated with β-rays. [15]

Processing offers to pericardium properties that render it suitable for sealing corneal tissue defects. The cell-free pericardial tissue composed of extracellular matrix proteins, which are generally conserved among species, can be easily used as a guide for host cell attachment, migration and proliferation. [16] This property is important for the promotion of corneal wound healing, as pericardium ensures a watertight closure of the perforation, while acting as a scaffold for stromal remodeling and epithelial surface closure. Moreover, the collagen network aquires a high mechanical resistance, it becomes easy to handle and its transparency allows visibility of the underlying tissues **(Figures 1c and d)**. Due to its equine origin, there is no risk of prion transmission. Finally, it is considered as biocompatible and is not expected to show any toxicity or hypersensitivity reaction. [16] All these qualities render lyophilized equine pericardium a reasonable off-label choice for corneal sealing, when donor grafts are not readily available.

First-line choices for tectonic repair of corneal perforations include gluing, conjuctival flaps, amniotic membrane and corneal transplantation in the form of penetrating keratoplasty, corneal patch graft, lamellar keratoplasty or tectonic epikeratoplasty. [1]

The extent of the perforation in our patient, as well as the instability of the surrounding cornea did not allow application of cyanoacrylate adhesive as this is indicated for smaller

defects. [17] Conjunctival flaps are not suitable for active keratitis with severe stromal thinning or in cases of a frank perforation, as they cannot always control the leakage. [18] Amniotic membrane or corneal allografts are established biomaterials for sealing corneal defects, however they were not available at that point in our clinic.

In the herein described case, equine pericardium patch was shown to be effective for sealing corneal perforations. A significant superficial and deep corneal neovascularization at the area of the pericardium graft especially on the left eye was established between the second and fifth month of follow-up **(Figures 2c and d)**. Since host bed vascularity is a cardinal risk factor for corneal graft rejection, [19] further management of neovascularization is essential prior to keratoplasty. Additional studies are needed to determine the overall safety and effectiveness of this biomaterial, as well as any differences in the properties and surgical outcomes among pericardial membranes from different species or newer tissue engineered biomaterials.

CONCLUSION

This is the first report on the use of equine pericardium for sealing corneal defects. Corneal integrity was achieved and maintained in both eyes of our patient with no signs of aqueous leak, hypotony, infection or recurrence. Considering its easy access and safety, it may be considered for the urgent management of corneal perforations when other donor tissue is not available.

REFERENCES

1. Jhanji V, Young AL, Mehta JS, Sharma N, Agarwal T, Vajpayee RB. Management of corneal perforation. Surv Ophthalmol. 2011; 56:522-38.
2. Lankaranian D, Reis R, Henderer J, Choe S, Moster MR. Comparison of single thickness and double thickness processed pericardium patch graft in glaucoma drainage device surgery. A single surgeon comparison of outcome. J Glaucoma. 2008; 17:48-51.
3. Raviv T, Greenfield DS, Liebmann JM, Sidoti PA, Ishikawa H, Ritch R. Pericardial patch grafts in glaucoma implant surgery. J Glaucoma. 1998; 7: 27-32.
4. Smith MF, Doyle JW, Ticrney JW Jr. A comparison of glaucoma drainage implant tube coverage. J Glaucoma. 2002; 11:143-7.
5. Weissgold DJ, Millay RH, Bochow TA. Rescue of exposed scleral buckles with cadaveric pericardial patch grafts. Ophthalmology. 2001; 108:753-8.
6. Gayre GS, Debacker C, Lipham W, Tawfik HA, Holck D, Dutton JJ. Bovine pericardium as a wrapping for orbital implants. Ophthal Plast Reconstr Surg. 2001; 17:381-7.
7. Novitskaya ES, Clifford L, Vivian AJ. Tutoplast pericardium patch graft for scleral thinning following strabismus surgery. Eye (Lond). 2013; 27:682-683.
8. Alio JL, Rodriguez AE, Martinez LM. Bovine pericardium membrane (Tutopatch) combined with solid platelet-rich plasma for the management of perforated corneal ulcers. Cornea. 2013; 32:619-24.
9. Khanna RK, Mokhtar E. Bovine pericardium in treating large corneal perforation secondary to alkali injuri: A case report. Indian J Ophthalmol. 2008; 56:429-430.
10. Centonze R, Agostini E, Massaccesi S, Toninelli S, Morabito L. A novel equine-derived pericardium membrane for dural repair: A preliminary, short-term investigation. Asian J Neurosurg. 2016; 11:201-5.
11. Uchimuro T, Fukui T, Shimizu A, Takanashi S. Mitral valve surgery in patients with severe mitral annular calcification. Ann Thorac Surg. 2016; 101:889-95.
12. Kubota H, Endo H, Noma M, Tsuchiya H, Yoshimoto A, Takahashi Y, Inaba Y, Nishino Y, Nunokawa M, Hosoi Y, Ikezoe T, Nemoto M, Makino Y, Nemoto Y, Matsukura M, Sugiyama

M, Abe N, Takeuchi H, Nagao G, Kondo E, Yanagida O, Yoshino H, Sudo K. Xenopericardial roll graft replacement for infectious pseudoaneyrysms and graft infections of the aorta. J Cardiothorac Surg. 2015; 10:133.

13. Di Stefano DA, Andreasi Bassi M, Cinci L, Pieri L, Ammirabile G. Treatment of a bone defect consequent to the removal of a periapical cyst with equine bone and equine membranes: Clinical and histological outcome. Minerva Stomatol. 2012; 61:477-90.
14. Materni A. Managing a vestibular infra-bony periodontal defect in the aesthetic zone through bone regeneration: A case report. Stomatolog. 2013; 19:30-5.
15. Escande Rémi, Nizar Khelil, Isabelle Di Centa, Caroline Roques, Maguette Ba, Fatima Medjahed-Hamidi, Frederic Chaubet, Didier Letourneur, Emmanuel Lansac and Anne Meddahi-Pelle (2011). Pericardial Processing: Challenges, Outcomes and Future Prospects, Biomaterials Science and Engineering, Prof. Rosario Pignatello (Ed.), ISBN: 978-953-307-609-6, InTech, Available from: http://www.intechopen.com/books/biomaterials-science-and-engineering/pericardial-processing-challengesoutcomes- and-future-prospects
16. Schmidt CE, Baier JM. Acellular vascular tissues: natural biomaterials for tissue repair and tissue engineering. Biomaterials. 2000; 21:2215-31.
17. Siatiri H, Moghimi S, Malihi M, et al. Use of sealant (HFG) in corneal perforations. Cornea. 2008; 27:988-91.
18. Arentsen J, Laibson PR, Cohen EJ. Management of corneal descemetoceles and perforations. Ophthalmic Surg. 1985; 16:29-33.
19. The collaborative corneal transplantation studies (CCTS). Effectiveness of histocompatibility matching in high-risk corneal transplantation. The Collaborative Corneal Transplantation Studies Research Group. Arch Ophthalmol. 1992; 110:1392-1403.